

EPILEPSY AND SUDDEN UNEXPECTED DEATH IN EPILEPSY?

Eat more fish! A group hypothesis

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Abstract – Epilepsy is the commonest serious neurological disorder and individuals with epilepsy are at higher risk of death than the general population and sudden unexpected death in epilepsy (SUDEP) is the most important direct epilepsy-related cause of death. Potential pathomechanisms for SUDEP are unknown, but it is very probable that cardiac arrhythmias during and between seizures play a potential role. The ultimate goal of SUDEP research is to develop methods to prevent it and nutritional aspects such as omega-3 fatty acid deficiency may have an interesting role in this scenario. Omega-3 fatty acids reduce the risk of cardiovascular mortality and are important for treating or preventing some neurological diseases, including epilepsy. A dietary modification or nutritional supplements increasing the ingestion of omega-3 fatty acids may help to “save the brain”.

KEY WORDS: epilepsy, sudden death, omega-3.

Epilepsia e morte súbita? Coma mais peixe! A hipótese de um grupo

Resumo – A epilepsia é uma das doenças neurológicas sérias mais comuns e está associada a um maior risco de morte do que o observado na população geral e a morte súbita em epilepsia é uma importante causa de morte relacionada à epilepsia. Os potenciais patomecanismos da morte súbita em epilepsia são desconhecidos, mas é bastante provável que arritmias cardíacas durante ou entre as crises tenham um papel preponderante. O objetivo final das pesquisas em morte súbita em epilepsia é o desenvolvimento de métodos que levem à sua prevenção e aspectos nutricionais, como a deficiência de ômega-3 pode ter um papel interessante neste contexto. A suplementação com ômega-3 reduz o risco de mortalidade de origem cardiovascular e é importante no tratamento e prevenção de algumas doenças neurológicas, incluindo a epilepsia. A modificação dietética ou a suplementação nutricional aumentando a ingestão de ômega-3 pode ajudar a “salvar o cérebro”.

PALAVRAS CHAVE: epilepsia, morte súbita, ômega-3.

SUDDEN UNEXPECTED DEATH IN EPILEPSY: GENERAL VIEW

Epilepsy is the commonest serious neurological disorder¹. Approximately, 3 percent of persons in the general population will have epilepsy at some point in their lives¹. Unfortunately, individuals with epilepsy are at higher risk of death than the general population and sudden unexpected death in epilepsy (SUDEP) is the most impor-

tant direct epilepsy-related cause of death². Some risk factors for SUDEP have been proposed, however, SUDEP is mainly a problem for patients with chronic uncontrolled epilepsy². Additionally, potential pathomechanisms for SUDEP are unknown, but it is very probable that cardiac arrhythmias during and between seizures play a potential role^{2,3}. Thus, while admitting the deficiencies in our current knowledge, the ultimate goal of SUDEP research is to

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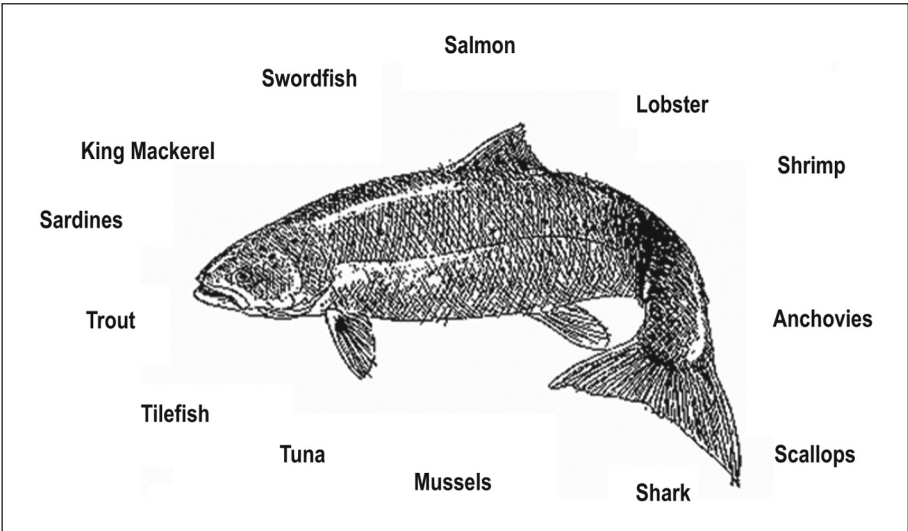


Figure. Main fish and shell fish rich in omega-3 fatty acids.

develop methods to prevent it. Following these reasoning, nutritional aspects such as omega-3 fatty acid deficiency may have an interesting role in this scenario.

ÔMEGA-3, EPILEPSY AND SUDDEN UNEXPECTED DEATH IN EPILEPSY

Polyunsaturated fatty acids are present at high levels in the brain⁴. The 04 polyunsaturated fatty acids are designed eicopentanoic acid (EPA) and decosahexanoic acid (DHA), which are n-3 fatty acids (omega-3); and dihomogammalinolenic acid (DGLA) and arachidonic acid (AA), which are n-6 fatty acids (omega-6), comprise over 10% (w/w) of the dry weight of the brain^{4,5}. In fact the brain, dietary consumption of the long-chain omega-3 fatty acids, commonly found in fish (fish oil) (Figure), is certainly a good way to improve the development of the brain (from the composition of cell membranes to cerebral function) and all omega-3 fatty acids reduce the risk of cardiovascular mortality (with an especially potent effect on sudden cardiac death) and are important for treating or preventing some neurological diseases, including epilepsy^{3,6}. Thus, as cardiovascular abnormalities during and between seizures are directly related to a high frequency of SUDEP^{2,3}, a possible relationship between omega-3 fatty acids, epilepsy, and SUDEP should be considered. Along these lines, several experimental studies have been shown that omega-3 fatty acids reduce neuronal excitability and may be useful in the nonpharmacological treatment of patients with epilepsy³⁻⁹. Very recently, our group was the first to demonstrate that chronic treatment with omega-3 fatty acids promotes neuroprotection and leads to prominent positive plastic changes in the hippocampal formation of rats with epilepsy³. From a clinical point of view, the first randomized, placebo-controlled parallel group study of

Table. Fish with low and high levels of methylmercury⁹⁻¹¹.

Low levels of methylmercury	High levels of methylmercury
Anchovies	Tuna
Atlantic herring	Shark
Atlantic mackerel	Tilefish
Wild salmon	Swordfish
Sardines	
Trout	

omega-3 supplementation in patients with chronic epilepsy showed only a transient effect on seizure frequency that was not confirmed by other research group, but additional trials are required^{3,10}. These results did not totally confirm that omega-3 fatty acids reduce the frequency of epileptic seizures in patients with intractable epilepsy; however, they established the safety of omega-3 supplementation in people with epilepsy¹⁰. Quite interesting, there is now great interest in epilepsy prevention, and recent work has shown that early treatment may block changes in the expression of ion channels¹¹. In these lines, n-3 fatty acids may be used for the prevention of SUDEP^{3,10}, as omega-3 fatty acids per se have been shown to reduce cardiac arrhythmias and sudden cardiac deaths, it is reasonable to think that omega-3 fatty acid supplementation in patients with refractory seizures may reduce seizures, seizure-associated cardiac arrhythmias and hence SUDEP^{3,10,12}.

Yes, fish is excellent for us. However, it is very important to remember that some kinds of fish contain contaminants that we'd rather not be eating. As we know, the major risk of fish consumption is its content of methylmercury¹³.

Considering the potential health risk of methylmercury consumption, an interesting question could be evaluated: Are we totally safe eating fish? It is clear that the concentration of methylmercury in fish is increased in predatory fish than non-predatory fish¹⁴. Thus, the best seafood choices are those with non predatory characteristics (Table)¹³⁻¹⁵.

In sum, a number of different dietary modifications and nutritional supplements may help prevent seizures or improve other aspects of health in patients with epilepsy. However, it is very important to emphasize that nutritional therapy (including omega-3 supplementation) is not a substitute for anticonvulsant medications. Overall, our research group strongly believes that fish is one of the most important foods we can choose for cardiovascular and brain health. The type of fish and seafood, the frequency of consumption, and the meal size are essential issues in the balance of benefits and risks of a regular consumption¹⁶. Concerning the cardioprotective effects of omega-3, it has long been believed that a daily intake of 3000 to 4000 mg of fish oil supplements or 2 to 3 servings of fatty fish per week are safe and effective in adults in general, included those with neurological diseases¹⁷. On the other hand, for individuals who want a diet with zero methylmercury but would like to enjoy the benefits of omega-3 fatty acids, there are always fish oil supplements or intake of foods such as walnuts or oils (flax, canola and soybean)^{16,18}. Neurologists should "save the brain" and prescribe fish again!

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